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10/521,111	09/23/2005	Donald Leonard Nicholas Cardy	056222-5068-US	6575

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EXAMINER	
THOMAS, DAVID C	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,111	CARDY ET AL.	
	Examiner	Art Unit	
	David C. Thomas	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-61* is/are pending in the application.

4a) Of the above claim(s) *40-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed July 12, 2007 is acknowledged. Claims 45-61 (newly added) will be examined on the merits. Claims 40-44 (currently amended) were previously withdrawn, and claims 40 and 44 are currently amended. Claims 1-39 have been canceled.

Claim Interpretation

2. Prior to examination of the claims, the claims must first be construed. Applicant has amended claim 45 to contain the limitation "whereby liquid applied to the sample receiving zone flows along the device passing sequentially through the extraction zone and amplification zone to the detection zone by capillary action through the porous matrix". This limitation represents functional or intended use limitations that do not impose additional structural limitations on the product. MPEP § 2111-14, first section, states "While features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function." Therefore, for the purposes of examination, the functional limitations set forth in the amended claim 45 are considered not to have structural impact and will not be treated as limitations to the claims.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 45-52, 54, 55 and 57-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Kozwich et al. (U.S. Patent No. 6,153,425).

Kozwich teaches a self-contained lateral flow assay device to test for the presence and/or amount of a nucleic acid sequence of interest in a sample (for overview, see column 4, lines 3-17 and 33-41) comprising:

(a) a sample receiving zone for contacting the device with a sample to be tested (sample is added through open end of top cylinder, column 7, lines 36-44 and lines 58-61 and Figure 1A and B, upper elongated and tapered chamber, part 2);

(b) a porous matrix which, at a proximal end, is in liquid communication with the sample receiving zone (the lateral flow device contains an opening and a solid phase porous membrane, Figure 2B, part 13 and Figure 5, part 22, through which liquid enters from a top cylinder that first received the sample, figure 2B, part 2 into a second receiving chamber, Figure 2B, part 16 and column 8, lines 37-44; a second porous membrane, the lateral flow strip, can also be in liquid communication with the sample receiving reservoir of cylinder 2 after rotation of the cylinder to allow contact of sample through opening, Figure 2B, part 13, and the solid phase porous membrane, Figure 5, part 22, into the detection chamber, Figure 2C, part 20 and parts 9 and 10 and column 8, lines 44-49);

(c) an extraction zone for extraction of nucleic acid from the sample (extraction takes place in upper chamber after closing lid with sealing lip in place preventing contact with lower chambers, column 7, lines 58-61 and column 8, lines 16-17; top cylinder is rotated to allow lysis buffer used in extraction to flow into collection reservoir

through aperture, column 7, lines 61-63, column 8, lines 18-19, and Figure 1B, parts 13 and 16);

(d) a nucleic acid amplification zone in liquid communication with the sample receiving zone, said extraction and amplification zones being located on the porous matrix (amplification occurs in upper chamber where sample is added after closing lid with sealing lip in place preventing contact with lower chambers, column 7, lines 58-61 and column 8, lines 16-17; top cylinder is rotated to allow wash buffers used in amplification step to flow into collection reservoir through aperture, column 7, lines 61-63, column 8, lines 18-19, and Figure 1B, parts 13 and 16; both extraction and amplification can take place on a solid surface such as a porous membrane, column 9, lines 22-36 and Figure 5, part 22); and

(e) a detection zone for detecting the product/s, directly or indirectly, of a nucleic acid amplification reaction performed in the nucleic acid amplification zone (detection takes place in lower chamber containing pad and detection strip, column 7, lines 44-47, Figure 1C, part 20, and Figure 2C, parts 9 and 10), said detection zone being in liquid communication with the amplification zone (the detection chamber is in fluid communication with the upper, amplification chamber when the upper chamber is rotated to allow sample to contact pad in lower chamber, column 7, line 64 to column 8, line 1, column 8, lines 20-29, Figure 1C, part 20 and Figure 2C, parts 9 and 10); whereby liquid applied to the sample receiving zone flows along the device passing sequentially through the extraction zone and amplification zone to the detection zone by capillary action through the matrix (the detection chamber contains absorbent pad and

detection strip made of nitrocellulose or other material that receives sample by wicking action from upper chamber containing sites of extraction and amplification, when aperture of upper chamber is positioned over detection chamber by rotation to allow sample to contact pad in lower chamber, column 7, line 64 to column 8, line 1, column 8, lines 20-29 and 45-49, Figure 1C, part 20 and Figure 2C, parts 9 and 10).

With regard to claim 46, Kozwich teaches a lateral flow assay device wherein the nucleic acid amplification comprises an isothermal amplification reaction (amplification can be performed by isothermal processes such as NASBA, column 11, lines 17-28, or strand displacement amplification (SDA), column 12, lines 13-18).

With regard to claims 47 and 48, Kozwich teaches a lateral flow assay device wherein the device comprises one or more reagents releasably bound on the porous matrix (the target nucleic acid, an essential reagent in amplification, is immobilized on the membrane after extraction and prior to amplification, and following the amplification step, the amplification reaction mixture is then eluted and allowed to flow into the detection chamber, column 9, lines 22 to 40, Figure 5, part 22 and Figure 2C, part 20).

With regard to claims 49 and 50, Kozwich teaches a lateral flow assay device comprising one or more reagents immobilized on the porous matrix (detection strip contains microparticles immobilized in region of strip that binds to and captures amplified target sample containing haptens after wicking onto strip after amplification in reaction chamber, column 8, lines 63-65 and Figure 6, part 24 and column 9, lines 41-44).

With regard to claim 51, Kozwich teaches a lateral flow assay device comprising a probe comprising nucleic acid releasably bound or immobilized on the porous matrix (probes used in cycling probe detection bind to microparticles when target is not present to produce signal indicating no target is present by binding in capture zone of strip, column 13, lines 27-37, column 14, lines 4-14 and Figure 12).

With regard to claim 52, Kozwich teaches a lateral flow assay device wherein the sample receiving zone comprises reagents suitable to perform a nucleic acid extraction step on a sample applied to the sample receiving zone (sample is first introduced into upper chamber containing reagents for extraction process, column 9, lines 16-25 and column 15, line 63 to column 16, line 8).

With regard to claim 54, Kozwich teaches a lateral flow assay device comprising means for interruption of flow, alteration of rate of flow, or alteration of flow path, of a liquid along the porous matrix within the device (flow of amplification target samples along strip will be interrupted when then reach capture zone to form visible dye line, column 9, lines 41-48 and Figure 6; flow of liquid onto strip can be stopped by rotation of upper cylinder relative to lower detection chamber such that aperture between chambers is sealed, such as in position A, column 7, line 64 to column 8, lines 6 and Figure 1A).

With regard to claim 55, Kozwich teaches a lateral flow assay device comprising means for altering the relative positions of two or more portions of the porous matrix, so as to affect the rate of flow of liquid from one portion to another (microparticles containing receptors for hapten can be located in different positions of porous matrix,

such as within pad, or in locations directly on strip, column 18, lines 13 to 18 and Figure 19, parts 39 and 58).

With regard to claim 57, Kozwich teaches an assay kit for performing an assay to test for the presence and/or amount of a nucleic acid sequence of interest in a sample, the kit comprising a lateral flow assay device according to claim 1, and a supply of at least one reagent required to perform the assay (lateral flow device includes an amplification reaction bead in a reaction bead chamber located in hinged cover of device, column 9, lines 28-32 and Figure 4, parts 11 and 12; extraction reagents are located in upper chamber for extracting samples added to upper chamber, column 9, lines 17-19).

With regard to claim 58, Kozwich teaches an assay kit comprising a supply of carrier liquid (water or buffer washes are provided to wash extracted nucleic acid bound to solid phase, column 9, lines 22-26; water is added to resuspend enzymes for amplification step, column 9, lines 27-36, followed by elution of amplified sample into detection chamber, column 9, lines 37-40).

With regard to claim 59, Kozwich teaches an assay kit wherein at least one reagent is provided dissolved and/or suspended in the carrier liquid (lysis buffer can either be in dry form and resuspended in liquid from sample, column 9, lines 17-19 or can be in liquid form, column 16, line 66 to column 17, line 4).

With regard to claims 60 and 61, Kozwich teaches a lateral flow assay device wherein the porous matrix consists of cellulose, cellulose derivatives and nylon and provided with a backing material (lateral flow strips are a membrane composed of nylon,

nitrocellulose or other suitable material, column 8, lines 23-25 and column 10, lines 50-52).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kozwich et al. (U.S. Patent No. 6,153,425) in view of Mao et al. (U.S. Patent No. 7,094,464).

Kozwich teaches the limitations of claims 45-52, 54, 55 and 57-61, as discussed above.

Kozwich does not teach a lateral flow assay device comprising dodecyl triethyl ammonium bromide or FTA paper.

Mao teaches materials and methods for DNA extraction and purification, including the used of lateral flow devices and flow through devices (column 5, lines 18-26 and column 17, lines 57-63). Mao also teaches DNA extraction reagents such as the surfactant dodecyltrimethylammonium bromide (DTAB) which can be used as coatings in such devices (column 10, lines 4-18).

Mao does not teach a lateral flow device to test for the presence and/or amount of nucleic acid sequence of interest in a sample comprising sample receiving, extraction, amplification and detection zones.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the self-contained lateral flow device of Kozwich with the DNA extraction reagents such as the surfactant dodecyltrimethylammonium bromide (DTAB) taught by Mao for use in lateral flow devices, since DTAB could easily be included in the dry lysing reagents taught by Kozwich. Thus, an ordinary practitioner would have been motivated to use a surfactant such as DTAB for DNA extraction in a self-contained lateral flow device since this reagent can be placed in the sample receiving cylinder and re-suspended in the liquid provided by the sample and used for extraction of nucleic acids suspended in a silica slurry (Kozwich, column 9, lines 12-25). Alternatively, the porous membrane could be coated with DTAB (Mao, column 10, lines 4-18) and used for solid phase extraction, with DNA bound to a porous membrane (Kozwich, column 9, lines 22-24 and Figure 5, part 22). Surfactants such as DTAB can easily and economically be made into layers

which exhibit strong binding ability to biomolecules such as nucleic acids (Mao, column 5, lines 27-35).

8. Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kozwich et al. (U.S. Patent No. 6,153,425) in view of Cardy et al. (WO 93/06240).

Kozwich teaches the limitations of claims 45-52, 54, 55 and 57-61, as discussed above.

Kozwich does not teach a lateral flow assay device wherein the amplification reaction comprises a SMART amplification reaction involving the sequence of interest in the formation of a three-way junction with two probe molecules.

Cardy teaches a SMART amplification reaction for testing for the presence of a nucleic acid sequence of interest in a sample comprising contacting the sample with a first and second probes such that the probes hybridize at substantially adjacent regions of the target and such that non-complementary portions of probes are annealed to each other to form three-way junction (p. 4, lines 21-31 and Figure 1, top).

Cardy does not teach a self-contained lateral flow device to test for the presence and/or amount of nucleic acid sequence of interest in a sample comprising sample receiving, extraction, amplification, and detection zones.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the self-contained lateral flow device of Kozwich with a SMART amplification reaction as taught by Cardy since the SMART method is easily compatible with the lateral flow device of Kozwich since it is powerful

and sensitive assay wherein the reagents can be placed in chambers the lateral flow device for release into the reaction chamber to react with target nucleic acid following extraction. Thus, an ordinary practitioner would have been motivated to use an alternative amplification process such as the SMART amplification reaction since this assay is highly sensitive and accurate, since extended probes will only be formed and detected in the presence of the sequence of interest (p. 6, lines 5-11). The SMART assay products can be easily amplified by any number of processes including isothermal processes to increase the signal (p. 6, lines 12-22), wherein such reagents can also be placed in the self-contained device, including primers containing the required haptens for detection during the lateral flow detection step.

Response to Arguments

9. Applicant's arguments filed July 12, 2007 have been fully considered but they are not persuasive.

Applicant argues that the rejection of claims 1, 2, 27-35 and 37-39 under 35 U.S.C. § 102(b) as being anticipated by Kozwich et al. (U.S. Patent No. 6,153,425) should be withdrawn since the reference no longer teaches all the features recited in the claims as amended. In particular, Applicant argues that Kozwich does not teach a lateral flow device but rather teaches a device comprising a lateral flow test strip for the final detection step, as well as other features and components. Applicant further argues that the device taught by Kozwich is more complex and structurally different from the device of the instant invention. The Examiner asserts that the device of Kozwich, while containing additional components not cited in the claims, comprises all the structural

features of the device set forth in the claims. Applicant further argues that the device of Kozwich, while functioning by capillary action of the sample from an upper to a lower cylinder, does not function by capillary flow through an extraction zone followed by flow through an amplification zone. As stated above, these limitations represent functional limitations that are not considered to have structural impact.

Applicant further argues that the device of Kozwich is not designed to perform extraction and amplification on a porous matrix, but only in suspension. The Examiner asserts that Kozwich teaches that both extraction and amplification can occur on a solid phase, in particular on a porous membrane (column 8, lines 34-41, column 9, lines 21-36 and Figure 5, part 22). Applicant further argues that Kozwich does not teach reagents releasably bound to a porous matrix, but rather a non-porous bead. As stated above, amplification can take place on a solid phase, and following the amplification step, the sample, including the original target DNA, is eluted into the detection chamber (column 9, lines 22 to 40, Figure 5, part 22 and Figure 2C, part 20). Applicant further argues that Kozwich does not teach a means for altering the relative positions of two or more portions of the porous matrix, so as to affect the rate of flow of liquid from one portion to another. As stated above, the lateral flow strip can contain microparticles conjugated with a receptor that is located on the porous membrane itself, but the device could be altered to contain the microparticles disposed in the absorbent pad instead (column 18, lines 13-18 and Figure 19, parts 39 and 58). Whether or not the alternate positions of the microparticles affect the rate of fluid flow is immaterial since the rate of flow is a functional limitation that is not considered to have structural impact. Finally,

Applicant argues that new claims 60 and 61 cite a porous matrix comprising cellulose, a cellulose derivative or nylon which Kozwich does not teach. As stated above, Kozwich does indeed teach a porous membrane comprising nitrocellulose or nylon (column 8, lines 23-25 and column 10, lines 50-52). There is no requirement by the claims that the same porous membrane also comprise both an extraction and amplification zone. Therefore, Kozwich teaches all the limitations of the amended claims and thus the 102(b) rejection is maintained for amended claims 45-52, 54, 55 and 57-61.

New claim 53 was amended to cite the limitation that the lateral flow device comprises dodecyl ammonium bromide (DTAB) or FTA paper, which Kozwich does not teach. However, upon further search, a new reference was found that teaches the use of DTAB in devices such as lateral flow or flow though devices (Mao et al. (U.S. Patent No. 7,094,464). Since Kozwich teaches the use of dry reagents for cell lysis and DNA extraction that can be re-suspended in the liquid of the sample in cylinder 2, it is obvious to combine the teaches of Mao and Kozwich, and therefore claim 53 is now rejected under 35 U.S.C. § 103(a) as being obvious over Kozwich in view of Mao.

Applicant then argues that the rejection of claim 36 (new claim 56) under 35 U.S.C. § 103(a) as being obvious over Kozwich in view of Cardy et al. (WO 93/06240) should be withdrawn since the combination of the references no longer teach all the limitations of the claims as amended. In particular, Applicant argues that since Kozwich does teach a lateral flow device according to the limitations cited in the claims and that Cardy does not make for the deficiencies of Kozwich. As stated above, Kozwich teaches a device that contains all the structural limitations of the claims as amended.

Therefore, since Carty teaches the additional limitations of claim 56 that is not separately argued, the 103 rejection is maintained.

Summary

10. Claims 45-61 are rejected. No claims are allowable.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320 and whose fax number is 571-273-3320. The examiner can normally be reached on 5 days, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David C. Thomas 9/19/07
David C. Thomas
Patent Examiner
Art Unit 1637

JEFFREY FREDMAN
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9/19/07